

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 15 February 2001 (15.02.01)	
International application No. PCT/GB00/02239	Applicant's or agent's file reference JNHS/SEB
International filing date (day/month/year) 09 June 2000 (09.06.00)	Priority date (day/month/year) 09 June 1999 (09.06.99)
Applicant SEYMOUR, Leonard, Charles, William et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

05 January 2001 (05.01.01)

in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer S. Mafla Telephone No.: (41-22) 338.83.38
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Co. for the designated Office (DO/US)
PATENT COOPERATION TREATY

PCT/GB00/02239

PCT

From the INTERNATIONAL BUREAU

**NOTIFICATION OF THE RECORDING
 OF A CHANGE**

(PCT Rule 92bis.1 and
 Administrative Instructions, Section 422)

To:

WILSON, Gunn, Skerrett
 Charles House
 148/9 Great Charles Street
 Birmingham B3 3HT
 ROYAUME-UNI

Date of mailing (day/month/year) 17 January 2001 (17.01.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference JNHS/SEB	
International application No. PCT/GB00/02239	International filing date (day/month/year) 09 June 2000 (09.06.00)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

CANCER RESEARCH CAMPAIGN
 TECHNOLOGY LIMITED
 Cambridge House
 6-10 Cambridge Terrace
 Regent's Park
 London NW1 4JL
 United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

HYBRID SYSTEMS LIMITED
 Birmingham Research Park
 Vincent Drive
 Birmingham B15 2SQ
 United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

The person in Box 1 has transferred the assignment to the person in Box 2

4. A copy of this notification has been sent to:

☒ the receiving Office ☒ the designated Offices concerned
☒ the International Searching Authority ☐ the elected Offices concerned
☐ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Authorized officer

Lazar Joseph Panakal

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

14

REC'D 02 OCT 2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference JNHS/LR	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/02239	International filing date (day/month/year) 09/06/2000	Priority date (day/month/year) 09/06/1999
International Patent Classification (IPC) or national classification and IPC A61K47/48		
Applicant HYBRID SYSTEMS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:
 - ☒ Basis of the report
 - ☐ Priority
 - ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Lack of unity of invention
 - ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Certain documents cited
 - ☐ Certain defects in the international application
 - ☐ Certain observations on the international application

Date of submission of the demand 05/01/2001	Date of completion of this report 28.09.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Vollbach, S Telephone No. +49 89 2399 8715 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02239

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

2,3,5-40 as originally filed

1,4 as received on 09/08/2001 with letter of 09/08/2001

Claims, No.:

32-34 as originally filed

1-31 as received on 09/08/2001 with letter of 09/08/2001

Drawings, sheets:

1/13-13/13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02239

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☒ the entire international application.

☐ claims Nos. .

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-31 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-31.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

Re ITEM III:

The "amended" claims and pages submitted by the Applicant are an unsuitable attempt to "disclaim" the prior art and thereby arbitrarily redefining certain claimed substances, thereby totally ignoring the proposals made by this Authority how a set of claims which could be examined could look like.

If these amendments should be seriously be taken into account the first and basic objection would be an objection for lack of unity. In view of the time schedule such a objection, however, can no longer be raised and prosecuted in this phase.

Anyhow, in accordance with the original clams also the new claims are objectionable for the same reasons. In addition, it is not even clear whether this "restricted" subject-matter has been searched at all (see the comments of the search examiner).

Therefore, this Authority does not see another possibility than to repeat the objections raised in the first opinion and, principally, establishing this report on the claims as originally filed.

1. Thus, this authority agrees with the search examiner that the claims (still) cover an uncountable number of various products for which no search and, consequently no examination can be carried out. This in principle applies for all claims.

From a different point of view and especially when considering the prior art which nevertheless has been found by the search examiner, the claimed "polymer modified biological elements" lack clarity since in none of the claims both components are clearly characterised by technical features and in most of the claims merely one of two components are defined.

In addition, in several of the claims one or the other component is merely characterised by the desired result to be achieved (see claims e.g. claims 6,12 etc). This, however, is in conflict with the requirements set out in Article 6 PCT.

2. Moreover, "polymer modified biological elements" in accordance with the claims are disclosed in the art (in this context and at present reference will be made merely to D1 to D4 (**D1:WO 98 05344 A** (BRIGHAM & WOMENS HOSPITAL ;SARKAR SAUMYENDRA N (US); DUBIN DANIEL) 12 February 1998 (1998-02-12) **D2:WO 98 19710 A** (SCHACHT ETIENNE HONORE ;ULBRICH KAREL (CZ); SEYMOUR

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/02239

LEONARD CHARLE) 14 May 1998 (1998-05-14) cited in the application **D3:WO 98 44143 A** (DELGADO CHRISTINA ;FRANCIS GILLIAN E (GB); POLYMASC PHARMACEUTICAL) 8 October 1998 (1998-10-08) cited in the application **D4:US-A-5 521 291** (BIRNSTIEL MAX L ET AL) 28 May 1996 (1996-05-28)), since these documents relate to those "modified materials which are exemplified in the present application, namely viruses) and consequently render the claimed subject-matter not novel and/or not inventive (Article 33.2 and Article 33.3 PCT).

In view of the objections raised above a detailed examination will only be possible once an amended set of claims is filed which overcomes the basic clarity and novelty objections.

3. In addition, regarding the prior art, it is necessary, also in order to avoid objections for lack of unity (Rules 13.1-13.3 PCT), that any claim relating to a compound (biological element) is restricted to the combination of one specific biological element (i.e. a specific virus) with one specific modifying polymer.

The applicant is informed that even with respect to such a specific combination, which when regarding the examples, might be a combination of an adenovirus with pHMPA, an inventive activity appears to be highly questionable in view of e.g. a combination of the disclosure of D1 or D3 in combination with D2 (wherein the polymer is described also in the context with a modified biological material, although not a virus).

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference JNHS/SEB	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/02239	International filing date (day/month/year) 09/06/2000	(Earliest) Priority Date (day/month/year) 09/06/1999
Applicant CANCER RESEARCH CAMPAIGN TECHNOLOGY LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-34 relate to an extremely large number of possible products and methods. In fact, the claims contain so many options, variables, possible permutations that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely products and methods have been searched recited in the examples.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02239

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EMBASE, BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A	WO 00 11202 A (RIORDAN CATHERINE E O ; GENZYME CORP (US); WADSWORTH SAMUEL C (US)) 2 March 2000 (2000-03-02) claims	
Y	WO 98 05344 A (BRIGHAM & WOMENS HOSPITAL ; SARKAR SAUMYENDRA N (US); DUBIN DANIEL) 12 February 1998 (1998-02-12) page 33, line 13 -page 34, line 8; claims; tables 1-3	1-34
X	US 5 521 291 A (BIRNSTIEL MAX L ET AL) 28 May 1996 (1996-05-28) claims; figure 1	1-34
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

30 January 2001

Date of mailing of the international search report

14/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Berte, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02239

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 19710 A (SCHACHT ETIENNE HONORE ;ULBRICH KAREL (CZ); SEYMOUR LEONARD CHARLE) 14 May 1998 (1998-05-14) cited in the application	1-34
X	page 6, line 18 -page 7, line 10; claims; examples page 15	1
Y	WO 98 44143 A (DELGADO CHRISTINA ;FRANCIS GILLIAN E (GB); POLYMASC PHARMACEUTICAL) 8 October 1998 (1998-10-08) cited in the application	1-34
X	page 7, line 14 -page 8, line 12; claims; examples 1,17-19,22	1
P,X	ROMANCZUK H ET AL: "MODIFICATION OF AN ADENOVIRAL VECTOR WITH BIOLOGICALLY SELECTED PEPTIDES: A NOVEL STRATEGY FOR GENE DELIVERY TO CELLS OF CHOICE" HUMAN GENE THERAPY, vol. 10, no. 16, 1 November 1999 (1999-11-01), pages 2615-2626, XP000879826 ISSN: 1043-0342 abstract	1
P,X	DASH, PHILIP R. ET AL: "Decreased binding to proteins and cells of polymeric gene delivery vector surface modified with a multivalent hydrophilic polymer and retargeting through attachment of transferrin" J. BIOL. CHEM. (2000), 275(6), 3793-3802 , XP002158846 abstract; figure 9	1-34
X	FASBENDER A ET AL: "COMPLEXES OF ADENOVIRUS WITH POLYCATIONIC POLYMERS AND CATIONIC LIPIDS INCREASE THE EFFICIENCY OF GENE TRANSFER IN VITRO AND IN VIVO" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 272, no. 10, 7 March 1997 (1997-03-07), pages 6479-6489, XP002060642 ISSN: 0021-9258 abstract	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/02239

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0011202 A	02-03-2000	AU 5685799 A	14-03-2000
WO 9805344 A	12-02-1998	AU 3737297 A	25-02-1998
US 5521291 A	28-05-1996	AT 187497 T	15-12-1999
		AU 669335 B	06-06-1996
		AU 2593292 A	03-05-1993
		CA 2114800 A	15-04-1993
		CN 1071457 A	28-04-1993
		DE 59209778 D	13-01-2000
		WO 9307282 A	15-04-1993
		EP 0535576 A	07-04-1993
		EP 0606280 A	20-07-1994
		FI 941473 A	30-03-1994
		HU 71322 A	28-11-1995
		HU 9500695 A	29-01-1996
		JP 7500009 T	05-01-1995
		MX 9205226 A	01-03-1993
		NO 941155 A	29-03-1994
		NZ 244291 A	26-07-1995
		ZA 9206767 A	11-06-1993
WO 9819710 A	14-05-1998	AU 4873997 A	29-05-1998
		EP 0941123 A	15-09-1999
WO 9844143 A	08-10-1998	AU 6881798 A	22-10-1998
		EP 0994959 A	26-04-2000

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
14 December 2000 (14.12.2000)

PCT

(10) International Publication Number
WO 00/74722 A3

(51) International Patent Classification⁷: **A61K 47/48**

(21) International Application Number: **PCT/GB00/02239**

(22) International Filing Date: **9 June 2000 (09.06.2000)**

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:
9913359.7 **9 June 1999 (09.06.1999)** **GB**

(71) Applicant (for all designated States except US): **HYBRID SYSTEMS LIMITED [GB/GB]; Birmingham Research Park, Vincent Drive, Birmingham B15 2SQ (GB).**

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SEYMOUR, Leonard, Charles, William [GB/GB]; CRC Institute for Cancer Studies, University of Birmingham, Birmingham B15 2TA (GB). FISHER, Kerry, David [GB/GB]; CRC Institute for Cancer Studies, University of Birmingham, Birmingham B15 2TA (GB).**

(74) Agent: **WILSON, Gunn, Skerrett; Charles House, 148/9 Great Charles Street, Birmingham B3 3HT (GB).**

(81) Designated States (national): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.**

(84) Designated States (regional): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).**

Published:

— *With international search report.*

(88) Date of publication of the international search report:
12 July 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **MODIFICATION OF BIOLOGICAL ELEMENTS**

(57) Abstract: A method of modifying the biological and/or physicochemical properties of biological elements such as viruses and other micro-organisms is disclosed in which the biological element is modified by providing it with a coating of a multivalent polymer having multiple reactive groups. This modification can enable some biological elements to be targeted or re-targeted to particular sites in a host biological system and can be useful in connection with viral vectors for gene therapy or antitumour therapy. In other cases the modification can be useful for enhancing or improving the efficiency of viruses or bacterial micro-organisms used for example in pest control, degradation and dispersal of oil deposits and various other industrial, environment or medical applications.

WO 00/74722 A3